Remarks

The Office Action mailed 2 May 2007 has been received and reviewed. Claim 9 having been amended, claims 7, 8, 23, 24, and 35-55 having been canceled, the pending claims are claims 1-3, 9-22, 25-34, and 56. Reconsideration and withdrawal of the rejections are respectfully requested.

Interview Summary

Applicants thank Examiner Hamud for the courtesy of the telephonic interview held August 16, 2007, including Examiner Hamud, inventor John Vasilakos, Ph.D., and Applicants' representative Christopher Gram.

Applicants discussed claims 1, 9, and 25 with regard to the rejections under 35 U.S.C. §112, first paragraph. Applicants' remarks centered on the knowledge of one skilled in the art at the time the invention was made. Those remarks are summarized in the comments provided below.

No firm agreement was reached. However, Applicants thank Examiner Hamud for the constructive discussion and guidance.

Claim Amendments

Claims 7, 8, 23, 24, and 35-55 have been canceled without prejudice.

Claim 9 has been amended to recite, in part, determining the TLR modulation profile of a test compound by providing an assay to detect modulation of a first TLR-mediated cellular activity and an assay to detect modulation of a second TLR-mediated cellular activity, performing the assay to detect modulation of the first TLR-mediated cellular activity using the test compound, performing the assay to detect modulation of the second TLR-mediated cellular activity using the test compound, and determining the extent to which the test compound modulates each TLR-mediated cellular activity. Support for the amendment may be found generally throughout Applicants' disclosure and in claim 1.

The 35 U.S.C. §112, Second Paragraph, Rejection

Claims 1-6, 9-22, and 25-34 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully traverse.

Claims 1, 9, and 25 are the independent claims. Claims 4-6 are canceled. Each of claims 2, 3, 10-22, and 26-34 depends, directly or indirectly, from one of claims 1, 9, and 25. Thus, remarks that refer to one or more of claims 1, 9, and 25 apply equally to all claims that depend from the indicated independent claim.

With regard to claim 1, the Office Action contends that the claims do not recite how to perform the assay or what activity or result to measure (Office Action, page 4). During the telephonic interview, Dr.Vasilakos explained that one skilled in the art is aware of a multitude of different assays (e.g., cytokine secretion, co-stimulatory marker production, functional assays, etc.) that can be employed to detect whether and to what extent a compound modulates TLR7- or TLR8-mediated cellular activity. The assays, how to perform the assays, and the endpoint (that which is being measured) for each assay are well known to those skilled in the art. Applicants therefore respectfully submit that claim 1 meets the requirements of 35 U.S.C. §112, second paragraph, and request that the rejection be withdrawn.

With regard to claim 9, the Office Action asserts that one skilled in the art would not know the positive steps of the claimed method. Claim 9 has been amended to recite steps that include providing an assay to detect modulation of a first TLR-mediated cellular activity and an assay to detect modulation of a second TLR-mediated cellular activity, performing the assay to detect modulation of the first TLR-mediated cellular activity using the test compound, performing the assay to detect modulation of the second TLR-mediated cellular activity using the test compound, and determining the extent to which the test compound modulates each TLR-mediated cellular activity. As noted with regard to claim 1, the assays, how to perform the assays, and the endpoint (that which is being measured) for each assay are well known to those

skilled in the art. Applicants respectfully submit, therefore, that claim 9 meets the requirements of 35 U.S.C. §112, second paragraph, and request that the rejection be withdrawn.

With regard to claim 25, the Office Action asserts that one skilled in the art would not know which human cell type to select and again asserts that one skilled in the art would not know which cellular activity to test for. During the interview, Dr. Vasilakos stated that one skilled in the art would, indeed, know which cell populations naturally express TLR7 and/or TLR8. Claim 25 does not recite testing the activity of the compound. Rather, claim 25 recites a method that makes practical use of the observation that certain TLR agonists modulate TLR-mediated cellular activity to varying degrees. Thus, claim 25 contemplates having knowledge of a plurality of TLR agonist compounds, knowing the TLR modulation profile of each compound, and knowing the desired TLR-mediated cellular activities one wishes to modulate. One skilled in the art can then select the compound that modulates TLR7-mediated cellular activity and TLR8-mediated cellular activity in the desired fashion to achieve the desired mix of TLR-mediated cellular activities from a human immune cell population, and then obtain that desired mix of TLR-mediated cellular activities by contacting the selected compound with the immune cell population. Applicants respectfully submit that claim 25 meets the requirements of 35 U.S.C. §112, second paragraph, and request that the rejection be withdrawn.

Therefore, Applicants respectfully submit that claims 1-6, 9-22, and 25-34 satisfy 35 U.S.C. §112, second paragraph, and request that the rejection be withdrawn.

The 35 U.S.C. §112, First Paragraph, Rejection (Enablement)

Claims 1-3, 25-34, and 56 stand rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Office Action acknowledges that Applicants' disclosure enables identifying a compound based on assays that includes culturing certain cells and measuring the expression of certain cytokines or co-stimulatory proteins. However, the Office Actions asserts

that Applicants' disclosure does not reasonably enable one skilled in the art to practice the full scope of the claims—i.e., does not reasonably enable the claimed methods using all possible assays to detect TLR-mediated cellular activity. Applicants respectfully traverse.

As noted above with regard to the rejections under 35 U.S.C. §112, second paragraph, Dr. Vasilakos explained during the telephonic interview that one skilled in the art recognizes that a multitude of routine, well known assays can be employed to determine whether and to what extent a compound modulates TLR-mediated cellular activity. The assays, how to perform the assays, and the endpoint (that which is being measured) for each assay are well known to those skilled in the art. Thus, one skilled in the art is able to practice the full scope of the subject matter recited in claims 1-3, 25-34, and 56.

Applicants respectfully submit that claims 1-3, 25-34, and 56 meet the enablement requirement of 35 U.S.C. §112, first paragraph, and request that the rejection be withdrawn.

The 35 U.S.C. §112, First Paragraph, Rejection (New Matter)

Claims 1 and 25 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. Specifically, the Office Action asserts that claims 1 and 25 recite "...human cells that naturally express TLR7" and "...human cells that naturally express TLR8", but that support for these limitations is lacking in Applicants' disclosure. Applicants respectfully disagree.

Examples 3 and 4 demonstrate selective modulation of plasmacytoid dendritic cells (pDCs) and myeloid dendritic cells (mDCs). The cell populations are obtained from peripheral blood mononuclear cells (PBMCs), obtained from human whole blood. The Office Action notes that a human source of the whole blood is not identified in Applicants' specification.

Human PBMCs are the source material for examples demonstrating cytokine induction in human cells by TLR agonist compounds in various patents cited in Applicants' disclosure (page 1, lines 22-32) and incorporated by reference at page 41, line 31 through page 42, line 2. PBMCs derived from human whole blood for cytokine induction assays is described, for

example, in U.S. Patent No. 6,667,312 at column 91, line 55 through column 92, line 9; U.S. Patent No. 6,677,348 at column 150, lines 6-29; U.S. Patent No. 6,677,349 at column 167, lines 7-30; and U.S. Patent No. 6,683,088 at column 67, line 58 through column 68, line 11.

Applicants respectfully request that the rejection of claims 1 and 25 under 35 U.S.C. §112, first paragraph, be withdrawn.

Summary

It is respectfully submitted that the pending claims 1-3, 9-22, 25-34, and 56 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted
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9/4/2007
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CERTIFICATE UNDER 37 CFR §1.8:
The undersigned hereby certifies that the Transmittal Letter and the paper(s), as described hereinabove, are being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to **Mail Stop RCE**, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 4th day of September, 2007, at 2:05 pm (Central Time).

By: Dani Mantz
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